

Claims

1. A 5'OT-EST polypeptide having a sequence selected from the group comprising the sequences set forth in any one of SEQ. ID. Nos. 2, 4 or 6, and sequences substantially homologous to any one of the polypeptides set forth in SEQ. ID. Nos. 2, 4 or 6.
2. The polypeptide of claim 1 comprising an amino acid sequence encoded by at least one exon selected from the group consisting of exons w, x, y and z as set forth in SEQ. ID. No. 16, or equivalents thereof as set forth in any one of SEQ. ID. Nos. 3 or 5.
3. The polypeptide of claim 2, which comprises an amino acid sequence encoded by at least part of exon w as set forth in SEQ. ID. No. 16, or equivalents thereof as set forth in any one of SEQ. ID. Nos. 3 or 5.
4. A mutant of a 5'OT-EST polypeptide according to any one of claims 1-3 which, *in vivo*, of modulates the obesity of an animal expressing it.
5. A mutant of any one of claims 1-7 claim 4, wherein the animal is a transgenic animal expressing the mutant as a result of transformation with a transgene.
6. A mutant of any one of claims 1-7 claim 4 or claim 5, which comprises the sequence PRPRSFSAPFSSQDS, or a sequence substantially homologous thereto.
7. A mutant of any one of claims 1-7 any one of claims 4 to 6 which comprises the sequence MLRALNRLAARPGGQPPTLLLLPVRGPRPRSFSAPFSSQDS, or a sequence substantially homologous thereto.
8. A nucleic acid encoding a 5'OT-EST polypeptide or mutant 5'OT-EST polypeptide of any one of claims 1-7.
9. A nucleic acid of any one of claims 1-7 claim 8, having a sequence selected from the group consisting of any one of SEQ. ID. Nos. 1, 3, 5, 7, 16 or 17; sequences which are hybridisable under stringent conditions with an oligonucleotide comprising 20 contiguous bases from any one of SEQ. ID. Nos. 1, 3, 5, 7, 16 or 17; sequences substantially homologous to any one of SEQ. ID. Nos. 1, 3, 5, 7, 16 or 17; and sequences complementary thereto.
10. A nucleic acid of any one of claims 1-7 claim 9, comprising the sequence
ATGTTGCGGGCTTTGAACCGCCTGGCCGCGCGGCCCGGGGGCCAGCCCCCAACCCT
GCTCCTTCTGCCCGTGCGCGGCCACGGCCCCGCTCATTCTCGGCTCCTTTTCCTCG
CAGGATAGC, or an equivalent sequence which encodes the same polypeptide having regard to the degeneracy of the nucleic acid code, or a sequence substantially homologous thereto.
11. A nucleic acid ~~vector~~ comprising a nucleic acid sequence of any one of claims 8 to 11.

12. A vector of any one of claims 1-7 claim 11 which is a cosmid vector.
13. A vector of any one of claims 1-7 claim 11 or claim 12 further comprising the sequences of the oxytocin (OT) gene, the vasopressin (AVP) gene and/or the human growth hormone (hGH) gene.
14. A vector of any one of claims 1-7 claim 12 having the structure of cVO14 as set forth in Figure 4 (SEQ. ID. No. 17).
15. A cell transformed with a vector of any one of claims 1-7 any one of claims 11 to 13.
16. A method for producing a 5'OT-EST polypeptide or a mutant 5'OT-EST polypeptide of any one of claims 1-7 any one of claims 1 to 7, comprising transforming a cell with a vector of any one of claims 1-7 any one of claims 11 to 13 and culturing the cell to produce the polypeptide.
17. A transgenic non-human animal expressing, as a result of transgene expression, a 5'OT-EST polypeptide or mutant 5'OT-EST polypeptide of any one of claims 1-7 any one of claim 1 to 7.
18. A transgenic animal of any one of claims 1-7 claim 17, which has been transformed with a vector of any one of claims 1-7 any one of claims 12 to 14.
19. A transgenic animal of any one of claims 1-7 claim 17 or claim 18, comprising more than one copy of the transgene.
20. A transgenic animal of any one of claims 1-7 any one of claims 17 to 19, which is a mammal.
21. A transgenic animal of any one of claims 1-7 claim 20 which is a rat.
22. A transgenic rat comprising at least four concatameric copies of a transgene having the structure of cVO14 as set forth in Figure 4 (SEQ. ID. No. 17).
23. A non-human mammal possessing the following obese phenotype: (i) a very late onset of obesity, (ii) a highly selective visceral distribution of fat developing on a normal rodent diet, without hyperphagia, (iii) an effect greatly preponderant in males, (iv) a predisposition to excessive dietary-fat induced obesity at an early age, before the phenotype becomes apparent on a normal diet, and (v) a dominant pattern of inheritance; the non-human mammal being obtainable by transformation with a vector of any one of claims 1-7 any one of claims 11 to 14.
24. A method of screening an animal of any one of claims 1-7 any one of claims 17 to 23 for changes in the animal's phenotype associated with obesity, comprising comparing the animal as

Sub
B2

a model for human late onset obesity, human dietary-fat associated juvenile obesity, human female post-menopausal obesity and/or human male infertility with an identical animal that has been subjected to environmental conditions or a drug.

25. A method for identifying a compound or compounds capable of modulating obesity and/or infertility in a mammal, comprising the steps of:

- a) exposing an animal of any one of claims 1-7 any one of claims 17 to 24 to the compound or compounds to be tested;
- b) determining the effect of the compound on the obesity and/or infertility phenotype; and
- c) selecting the compound or compounds which are capable of modulating the obesity and/or infertility phenotype in the desired manner.

26. A method for producing a compound or compounds capable of modulating obesity and/or infertility in a mammal, comprising the steps of:

- a) exposing an animal of any one of claims 1-7 any one of claims 17 to 24 to the compound or compounds to be tested;
- b) determining the effect of the compound on the obesity and/or infertility phenotype;
- c) selecting the compound or compounds which are capable of modulating the obesity and/or infertility phenotype in the desired manner; and
- d) producing the compound or compounds by conventional isolation or synthesis techniques.

27. A method for identifying a candidate compound capable of influencing lipid transport, comprising the steps of:

- a) contacting 5'OT-EST polypeptide with a candidate compound or compounds and determining which candidate compound or compounds is capable of interacting with 5'OT-EST;
- b) optionally, testing candidate compounds which interact with 5'OT-EST in a method of any one of claims 1-7 claim 25.

546E6 28. A diagnostic reagent for the detection of mutations, polymorphisms or other changes in 5'OT-EST which may predispose an individual to obesity.

29. A method of screening a tissue derived from a transgenic animal of any one of claims 1-7 any one of claims 17 to 24 in a screen to identify a genetic cause of obesity, comprising the steps of:

- a) isolating one or more gene products from tissue derived from a transgenic animal of any one of claims 1-7 any one of claims 17 to 24; and
- b) determining whether the expression of a gene product is correlated with obesity.

add E? > 